

Epidemiology and Risk of Coronavirus Disease 2019 Among Travelers at Airport and Port Quarantine Stations Across Japan: A Nationwide Descriptive Analysis and an Individually Matched Case-Control Study

Motoyuki Tsuboi,¹ Masahiko Hachiya,³ Hiroshi Ohtsu,² Hidechika Akashi,⁴ Chiaki Miyoshi,¹ and Tamami Umeda⁵

¹Department of Human Resource Development, Bureau of International Health Cooperation, National Center for Global Health and Medicine, Tokyo, Japan; ²Department of Data Science, Center for Clinical Sciences, National Center for Global Health and Medicine, Tokyo, Japan; ³Department of Global Health Policy and Research, Bureau of International Health Cooperation, National Center for Global Health and Medicine, Tokyo, Japan; ⁴Department of Health Planning and Management, Bureau of International Health Cooperation, National Center for Global Health and Medicine, Tokyo, Japan; and ⁵Bureau of International Health Cooperation, National Center for Global Health and Medicine, Tokyo, Japan

Background. The epidemiology and risk of coronavirus disease 2019 (COVID-19) among travelers at international borders remain unclear.

Methods. We conducted descriptive and individually matched case-control studies using a nationwide register for COVID-19 testing of travelers from 3 August to 31 October 2020 at airport/port quarantine stations across Japan. Case patients, defined as travelers positive for COVID-19 on arrival, were individually matched with 4 controls for arrival date and airport or port. We assessed associations between test positivity and traveler characteristics using conditional logistic regression analysis.

Results. Overall, 157 507 travelers arriving from 146 countries/areas at 17 quarantine stations across Japan were tested for COVID-19. The percentage of test positivity during the study period was 0.35%. In the case-control study, with 536 case patients and 2144 controls, we found evidence of lower test positivity in travelers aged 3–19 years, female travelers, and travel corridor users (adjusted odds ratio [95% confidence interval], 0.36 [.22–.60], 0.71 [.56–.89], and 0.48 [.30–.77], respectively), whereas higher positivity was associated with arrival from South-East Asia (1.88 [1.33–2.65]) or lower-middle- or low-income countries (2.46 [1.69–3.58] and 7.25 [2.22–23.66], respectively), any symptom (4.08 [1.43–11.65]), and nasopharyngeal compared with saliva sampling (2.75 [1.85–4.09]). A higher 14-day average incidence in the countries of stay was also associated with higher test positivity (1.64 [1.16–2.33] and 3.13 [1.88–5.23] for those from countries and areas where the 14-day average incidence was from 10 to <100 and ≥100 cases per million, respectively).

Conclusions. These findings justify travel restrictions based on the epidemic situation in countries of stay, although underestimation of the epidemic in lower-income countries should be considered. A strict travel corridor could also reduce the risk of COVID-19 importation.

Keywords. COVID-19; airport; port; quarantine station; travel corridor.

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported in Wuhan, China, in late 2019. Thereafter, the disease rapidly spread worldwide via travelers, and the World Health Organization (WHO) declared a pandemic on 11 March 2020. Most countries have adopted control measures to mitigate the transmission of SARS-CoV-2, including border closures to prevent the entry of infected travelers [1, 2].

The association between migratory movements and COVID-19 outbreaks and SARS-CoV-2 in-flight transmission has been reported in some studies [3–6]. Nevertheless, the impact of border control in containing the global spread of COVID-19 and the best approach to lift these restrictions safely are still not established. One study found that screening of travelers at entry and isolation of test-positive cases reduced the average case importation by >90% and that the average reduction in secondary cases was 88.2%–92.1% [7], whereas findings of another study suggested that 90% travel restriction alone only modestly affected the epidemic trajectory [8]. Other studies have identified situations in which travel restrictions are considered effective, such as countries with low COVID-19 incidence and large numbers of arrivals from other countries [9, 10]. However, the existing evidence is based exclusively on modeling studies.

After the emergence of new variants of SARS-CoV-2, such as VOC-202012/01 and 501Y.V2, many countries have

Received 11 June 2021; editorial decision 22 July 2021; published online 28 July 2021.

Correspondence: M. Tsuboi, Department of Human Resource Development, Bureau of International Health Cooperation, National Center for Global Health and Medicine, 1-21-1 Toyama Shinjuku-ku, Tokyo 162-8655, Japan (mtsuboi@it.ncgm.go.jp).

Clinical Infectious Diseases® 2021;XX(X):1–9

© The Author(s) 2021. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com. <https://doi.org/10.1093/cid/ciab659>

strengthened border control measures, including pretravel and posttravel screening tests, to avoid importation of these variants. Considering the limited capacity of screening tests, compared with the large number of travelers after widespread reopening of international borders, a more precise assessment of COVID-19 epidemiology and the high- and low-risk populations at airport and port quarantine stations is urgently needed for prioritization. To inform policy-making decisions regarding international travel restrictions and easing of border control, we assessed the association between COVID-19 test positivity on arrival and traveler characteristics, including the epidemic situation in the countries of stay and the use of travel corridors between Japan and other countries, an arrangement whereby the governments of 2 countries allow people to travel directly between countries without observing some travel restrictions.

METHODS

Study Design and Participants

We conducted a descriptive study and an individually matched case-control study using a register provided by the Ministry of Health, Labour and Welfare, Japan, for results of COVID-19 testing and characteristics of travelers who arrived from 3 August to 31 October 2020 at airport or port quarantine stations across Japan. During the study period, the government of Japan applied entry ban to 146 or more countries and areas (146 between 3 and 29 August, and 159 between 30 August and 31 October) [11]. All travelers having stayed in the designated countries and areas within 14 days before their arrival in Japan were tested for COVID-19 to isolate positive travelers, and their results and characteristics were registered.

In parallel, measures for easing travel restrictions began on 29 July 2020, using travel corridor frameworks called Business Track and Residence Track, which enabled cross-border travel between countries where the COVID-19 epidemic was well controlled and Japan under additional quarantine measures, such as a certificate of pretravel test results with a nucleic acid amplification test (NAT; ie, polymerase chain reaction [PCR] or loop-mediated isothermal amplification test) or a quantitative antigen test, retaining location data for 14 days after entering Japan, and submission of their schedule of activities in Japan [12]. This study used all registered data and covered the initial period of easing travel restrictions.

In the individually matched case-control study to analyze the association between COVID-19 diagnosis at airport and port quarantine stations and traveler characteristics, we individually matched each case patient with 4 controls, with respect to arrival date and arrival airport or port to control for differences in screening strategies by time and place. Before selecting case patients and controls, we excluded from the register those who visited multiple countries within 14 days before arrival in Japan and those with missing values in any of the matching or

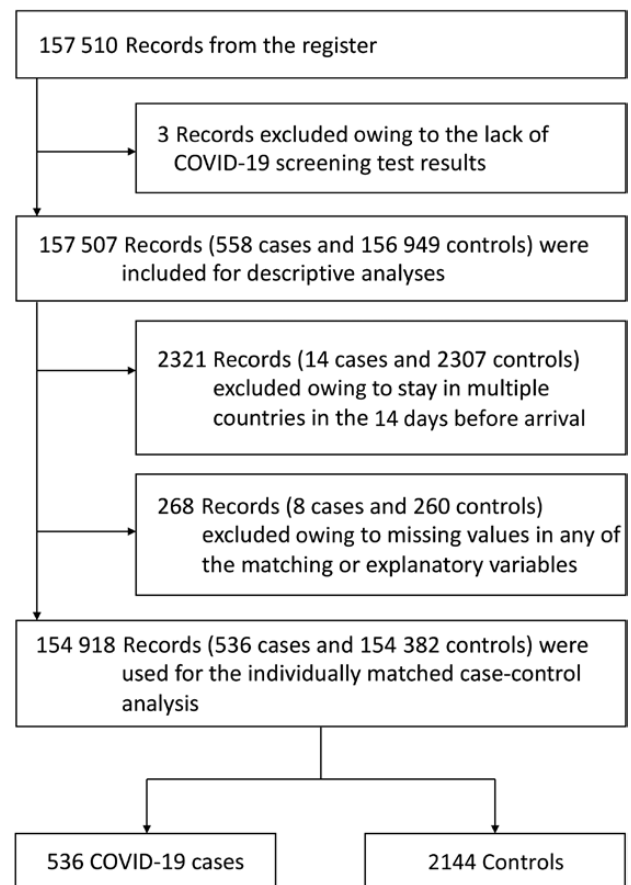


Figure 1. Flow chart for the selection process of enrolled travelers. Abbreviation: COVID-19, coronavirus disease 2019.

explanatory variables (Figure 1). Case patients were defined as travelers who were diagnosed with COVID-19 on arrival at airport and port quarantine stations across Japan, including 5 major airports (Narita International, Tokyo International, Kansai International, Chubu Centrair International, and Fukuoka Airports). Controls were COVID-19–negative travelers.

We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting case-control studies (Supplementary Table 1) [13]. This study was approved by the Institutional Review Board for Clinical Research at the National Center for Global Health and Medicine in Tokyo (no. NCGM-G-003664-00). Written informed consent was waived by the board because the data were anonymized.

Data Collection

We collected relevant information from the national register of COVID-19 testing for border control at airport and port quarantine stations across Japan: age, sex, nationality, arrival airport or port, arrival date, countries and areas where the travelers stayed within 14 days before arrival in Japan, any symptom on arrival, use of travel corridors, whether travelers were seafarers

or not, diagnostic methods used, specimen type for sampling, and test result. The Business Track and Residence Track are for business persons, but a subsequently introduced framework starting on 1 October 2020 for students, dependents, and other people from all over the world has the same procedure as that for the Residence Track; therefore, it was counted toward the Residence Track category. The travelers seafarer status was collected because the percentage of COVID-19 test positivity (ie, the proportion of travelers testing positive for COVID-19) seemed to be high among seafarers, based on prior experience at quarantine stations in Japan.

Since the first day of this study, 3 August 2020, the NAT, which was used as the screening test for COVID-19, was completely replaced by a quantitative antigen detection test (Lumipulse SARS-CoV-2 Ag; Fujirebio) at 4 of the 5 major airport quarantine stations, other than Fukuoka Airport, where the screening test was thoroughly shifted to the antigen detection test on 16 September 2020 [14, 15]. If the result of the antigen detection test was inconclusive even after the replacement, NAT was performed for confirmation. Among the other 12 smaller airports and ports accounting for 0.2% (298 of 157 507) of all test results, 3 replaced the screening method at the same time as the 4 major airports, 2 changed it during the study period, like Fukuoka Airport, and 7 continued to use the NAT for screening.

Outcome and Explanatory Variables

For the individually matched case-control study, we considered the COVID-19 test result as the outcome variable. Explanatory variables included age group, sex, nationality (Japanese or non-Japanese), use of travel corridors, seafarer status, symptoms on arrival in Japan, specimen type for sampling (nasopharyngeal or saliva), as well as WHO regions and income levels according to the World Bank classification (low, lower-middle, upper-middle, and high) of the countries and areas where travelers stayed within 14 days before arrival in Japan [16]. We also used the 14-day average incidence (number of newly reported cases per million) in the countries and areas as an explanatory variable, which was obtained from the WHO Coronavirus Disease Dashboard [17] and United Nations World Population Prospects 2019 [18] to reflect the epidemic situation in the country during the incubation period of the traveler (< 10, 10 to < 100, and ≥ 100 COVID-19 cases per million).

Statistical Analysis

We calculated unadjusted and adjusted matched odds ratios (ORs) with 95% confidence intervals (CIs), using conditional logistic regression analysis to assess associations between COVID-19 test positivity at quarantine stations and characteristics of travelers. Differences were considered significant at $P < .05$. In multivariable models, we included all explanatory variables and determined variance inflation factors to assess multicollinearity. Interactions between explanatory variables

were assessed with likelihood ratio tests. We also conducted a sensitivity analysis in the matched case-control study, assessing the influence of the data from Fukuoka Airport, which adopted a different screening measure until the middle of the study period. All statistical analyses were performed using Stata/IC software, version 16.1.

RESULTS

Overall, we obtained the records of 157 510 travelers who arrived from 146 countries and areas and were tested for COVID-19 at 17 airport and port quarantine stations across Japan. After exclusion of 3 travelers (0.002%) owing to lack of COVID-19 screening test results, 157 507 travelers were analyzed descriptively. Before matching, we excluded 2321 travelers (1.5%) who visited ≥ 2 countries in the 14 days before arrival in Japan and 268 (0.2%) with missing values in any of the matching or explanatory variables. As a result, we included 536 case patients and 2144 controls for the individually matched case-control study (Figure 1).

First, we descriptively analyzed the characteristics of 157 507 travelers with a median age of 34 years (interquartile range, 24–47 years; range, 0–96) (Table 1). Of these travelers, 59.8% (94 151 of 157 381) were male, and 44.1% (69 485 of 157 405) were Japanese nationals. Almost all travelers (99.8% [157 209 of 157 507]) were tested at 5 major airports, and all positive COVID-19 screening test results were obtained at these 5 airports. Of all travelers tested, 155 087 (98.5%) were tested only with the quantitative antigen detection test, and 558 (0.35%) were COVID-19 positive.

The time trends of the numbers of travelers tested and the percentage of COVID-19 test positivity are presented in Figure 2A. Compared with August, the number of travelers tested in October increased 1.5-fold (from 43 616 to 65 821), especially among non-Japanese travelers (1.3-fold increase in Japanese [from 20 719 to 25 998] vs 1.7-fold in non-Japanese travelers [from 22 850 to 39 787]), after the introduction of an additional framework that allowed cross-border travel for students, dependents, and others. The increasing trend of travel corridor users is also shown in Figure 2B and Supplementary Figure 1. However, the percentage of COVID-19 test positivity among tested travelers slightly decreased from 0.4% (168 of 43 616) in August to 0.3% (217 of 65 821) in October.

We also examined the association between the percentage of COVID-19 test positivity and age (Figure 3A), as well as the percentage of COVID-19 test positivity at quarantine stations by countries and areas where the travelers stayed in the 14 days before arrival in Japan (Figure 3B and Supplementary Figures 2 and 3).

In the individually matched case-control study, the median ages of travelers (interquartile range) were 35 (26–48) years for case patients and 35 (25–48) years for controls, and 70.7% and

60.3% of case patients and controls, respectively, were male. Other characteristics are presented in Table 2.

When we assessed the association between COVID-19 test positivity and baseline characteristics (Table 2), we found some

evidence of lower test positivity in travelers aged 3–19 years, female travelers, and travel corridor users (adjusted OR [95% CI], 0.36 [.22–.60], 0.71 [.56–.89], and 0.48 [.30–.77], respectively). The results also suggested evidence of higher

Table 1. Baseline Characteristics of Travelers Tested for Coronavirus Disease 2019 on Arrival at Airport and Port Quarantine Stations Across Japan

Characteristic	Travelers, No. (%)		
	Tested for COVID-19	Testing Positive for COVID-19	Proportion of Travelers Positive for COVID-19, %
Age, y (n = 157 484)			
<2	3737 (2.37)	26 (4.66)	0.70
3–19	16 153 (10.26)	19 (3.41)	0.12
20–39	76 586 (48.63)	281 (50.36)	0.37
40–64	54 969 (34.90)	214 (38.35)	0.39
≥65	6039 (3.83)	18 (3.23)	0.30
Sex (n = 157 381)			
Male	94 151 (59.82)	397 (71.15)	0.42
Female	63 230 (40.18)	161 (28.85)	0.25
Nationality^a (n = 157 405)			
Japanese	69 485 (44.14)	208 (37.28)	0.30
Non-Japanese	87 920 (55.86)	350 (62.72)	0.40
Arrival airport or port (n = 157 507)			
NRT	87 911 (55.81)	324 (58.06)	0.37
HND	44 496 (28.25)	145 (25.99)	0.33
KIX	21 083 (13.39)	75 (13.44)	0.36
NGO	1831 (1.16)	2 (0.36)	0.11
FKU	1888 (1.20)	12 (2.15)	0.64
Others	298 (0.19)	0 (0)	0
No. of countries and areas^b (n = 157 507)			
1	155 186 (98.53)	544 (97.49)	0.35
≥2	2321 (1.47)	14 (2.51)	0.60
WHO region^{b,d} (n = 155 186)			
Africa ^c	1182 (0.76)	4 (0.74)	0.34
Americas	34 528 (22.25)	91 (16.73)	0.26
Eastern Mediterranean	4726 (3.04)	28 (5.15)	0.59
Europe	24 981 (16.10)	98 (18.01)	0.39
South-East Asia	17 732 (11.43)	116 (21.32)	0.65
Western Pacific	72 040 (46.42)	207 (38.05)	0.29
Income level of countries and areas^{b,d} (n = 155 183)			
High	75 465 (48.63)	193 (35.48)	0.26
Upper middle	41 690 (26.87)	108 (19.85)	0.26
Lower middle	37 580 (24.22)	234 (43.01)	0.62
Low ^e	448 (0.29)	9 (1.65)	2.01
14-day average COVID-19 incidence in countries and area, newly reported cases per million people^{b,d} (n = 155 186)			
<10	67 271 (43.35)	153 (28.12)	0.23
10 to <100	48 522 (31.27)	246 (45.22)	0.51
≥100	39 393 (25.38)	145 (26.65)	0.37
Any symptoms (n = 157 495)			
No	156 813 (99.57)	548 (98.21)	0.35
Yes	682 (0.43)	10 (1.79)	1.47
Specimen type (n = 157 493)			
Saliva	147 017 (93.35)	465 (84.55)	0.32
Nasopharyngeal	10 476 (6.65)	85 (15.45)	0.81
Use of travel corridor framework (n = 157 507)			
None	141 055 (89.55)	526 (94.27)	0.37
Residence Track	15 963 (10.13)	31 (5.56)	0.19

Table 1. Continued

Characteristic	Travelers, No. (%)		
	Tested for COVID-19	Testing Positive for COVID-19	Proportion of Travelers Positive for COVID-19, %
Business Track	489 (0.31)	1 (0.18)	0.20
Seafarer ^a (n = 157 507)			
No	140 793 (89.39)	447 (80.11)	0.32
Yes	16 714 (10.61)	111 (19.89)	0.66
Total	157 507 (100)	558 (100)	0.35

Abbreviations: COVID-19, coronavirus disease 2019; FUKU, Fukuoka Airport; HND, Tokyo International Airport (Haneda Airport); KIX, Kansai International Airport; NGO, Chubu Centrair International Airport; NRT, Narita International Airport; WHO, World Health Organization.

^aTravelers with both Japanese and non-Japanese nationalities were classified as non-Japanese.

^bCountries and areas where travelers stayed within 14 days before arrival.

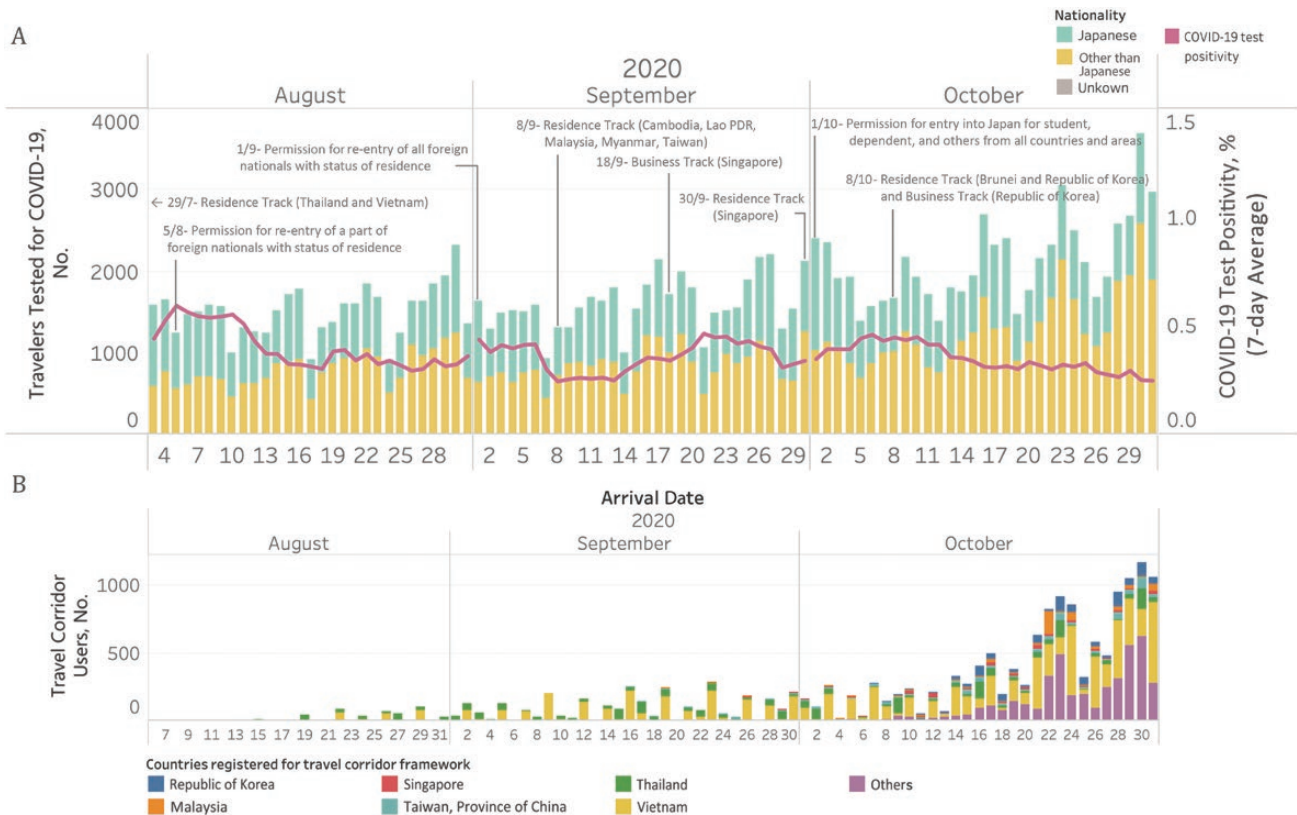
^cOf 448 travelers from low-income countries, 240 (53.6%) were from the Eastern Mediterranean region, followed by 176 (39.3%) from the African region. On the other hand, 747 (63.2%) of 1182 travelers from the African region were from lower-middle-income countries, followed by 210 (17.8%) from upper-middle-income countries and 176 (14.9%) from low-income countries. Only 12.1% was the overlap of travelers from African region and low-income countries.

^dAmong travelers who stayed in only 1 country within 14 days before arrival.

^eDuring the study period, seafarers also entered Japan through airports (eg, as replacement staff) and were tested for COVID-19.

COVID-19 test positivity in travelers who had any symptoms on arrival (adjusted OR [95% CI], 4.08 [1.43–11.65]), those sampled using nasopharyngeal swab versus saliva samples (2.75 [1.85–4.09]), those from severely affected countries and areas where the 14-day average incidence was from 10 to <100 and ≥100 cases per million (1.64 [1.16–2.33] and 3.13 [1.88–5.23],

respectively), and those arriving from lower-middle- or low-income countries (2.46 [1.69–3.58] and 7.25 [2.22–23.66], respectively). Among 6 WHO regions, higher COVID-19 test positivity was significantly associated with a stay in South-East Asia (adjusted OR [95% CI], 1.88 [1.33–2.65]) compared with a stay in the Western Pacific region. No meaningful interaction



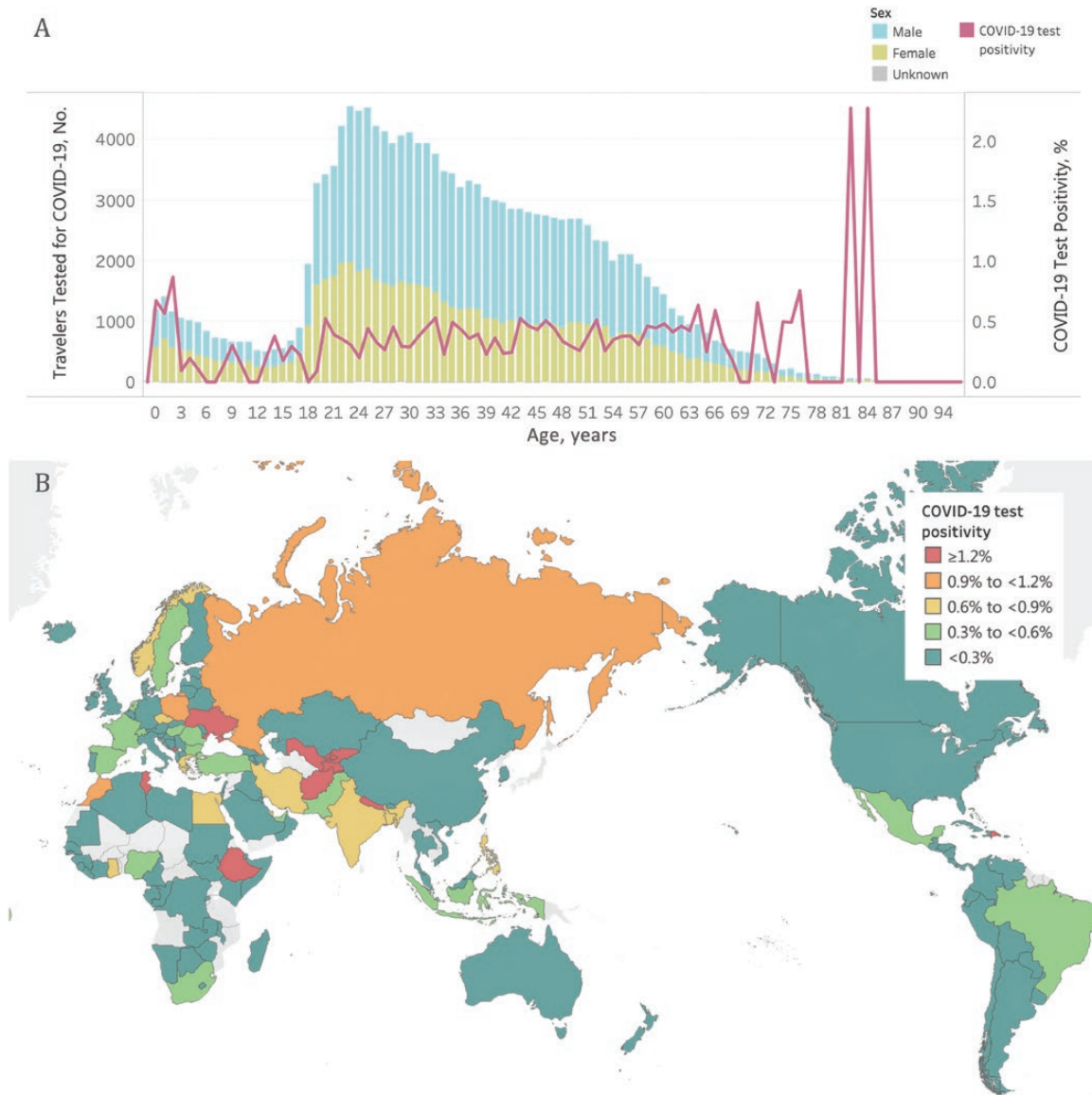


Figure 3. Percentage of coronavirus disease 2019 (COVID-19) test positivity at quarantine stations by age and countries and areas. *A*, Age distribution of the number of travelers tested by sex and the percentage of test positivity. Compared with travelers aged ≥ 20 years, those aged < 20 years showed a low proportion of positive test results, except for those aged 0–2 years, who showed a higher proportion. The higher percentage of positivity among elderly travelers was considered to be due to the small number of travelers tested. *B*, COVID-19 test positivity at quarantine stations by countries and areas where travelers stayed.

was found among explanatory variables. The results of the sensitivity analysis showed little difference between results with or without data from Fukuoka Airport ([Supplementary Table 2](#)).

DISCUSSION

To the best of our knowledge, this is the first study using individual-level nationwide quarantine data to assess the association between traveler characteristics and COVID-19 screening test positivity at airport and port quarantine stations in a country. During the study period, the percentage of COVID-19 test positivity decreased slightly from 0.4% in August to 0.3% in October 2020, while the number of travelers tested increased

1.5-fold. COVID-19 test positivity was low among children and adolescents (aged 3–19 years), female travelers, and travel corridor framework users. On the other hand, the positivity was high among travelers who arrived from South-East Asia or lower-middle- or low-income countries and among those with any symptom. Severe epidemics in the countries of stay were also associated with higher test positivity in travelers.

The positivity of COVID-19 screening tests at airport and port quarantine stations across Japan was low, at 0.35%, from August to October 2020. After the easing of travel restrictions in Japan, beginning on 29 July 2020, the number of travelers tested increased gradually from August to September. Once an

Table 2. Characteristics of Case Patients and Controls and Their Association With Coronavirus Disease 2019 Screening Test Positivity at Airport Quarantine Stations Across Japan

Characteristic	Travelers, No. (%)		Crude OR		Adjusted OR ^a	
	Case Patients (n = 536)	Controls (n = 2144)	OR (95% CI)	PValue	OR (95% CI)	PValue
Age, y						
≤2	26 (4.9)	43 (2.0)	2.30 (1.38–3.82)	<.001	1.04 (.54–2.01)	.91
3–19	19 (3.5)	208 (9.7)	0.35 (.21–.57)	<.001	0.36 (.22–.60)	<.001
20–39	270 (50.4)	1027 (47.9)	1 (Reference)	...	1 (Reference)	...
40–64	206 (38.4)	773 (36.1)	1.01 (.83–1.24)	.90	1.04 (.83–1.30)	.74
≥65	15 (2.8)	93 (4.3)	0.61 (.35–1.08)	.09	0.69 (0.37–1.27)	.24
Sex						
Male	379 (70.7)	1293 (60.3)	1 (Reference)	...	1 (Reference)	...
Female	157 (29.3)	851 (39.7)	0.63 (.51–.77)	<.001	0.71 (.56–.89)	.003
Nationality^b						
Japanese	195 (36.4)	892 (41.6)	1 (Reference)	...	1 (Reference)	...
Non-Japanese	341 (63.6)	1252 (58.4)	1.25 (1.02–1.52)	.03	1.05 (.82–1.34)	.69
14-day average COVID-19 incidence in countries and areas,^c newly reported cases per million people						
<10	152 (28.4)	932 (43.5)	1 (Reference)	...	1 (Reference)	.
10 to <100	239 (44.6)	644 (30.0)	2.28 (1.81–2.86)	<.001	1.64 (1.16–2.33)	.006
≥100	145 (27.1)	568 (26.5)	1.57 (1.22–2.01)	<.001	3.13 (1.88–5.23)	<.001
WHO region^c						
Africa	4 (0.8)	18 (0.8)	1.10 (.37–3.28)	.87	0.66 (.20–2.13)	.49
Americas	91 (17.0)	482 (22.5)	0.93 (.71–1.22)	.61	0.63 (.36–1.10)	.10
Eastern Mediterranean	28 (5.2)	74 (3.5)	1.87 (1.18–2.97)	.007	1.46 (.85–2.52)	.17
Europe	97 (18.1)	314 (14.7)	1.53 (1.16–2.01)	.002	1.40 (.89–2.22)	.15
South-East Asia	116 (21.6)	268 (12.5)	2.14 (1.63–2.80)	<.001	1.88 (1.33–2.65)	<.001
Western Pacific	200 (37.3)	988 (46.1)	1 (Reference)	...	1 (Reference)	...
Income level of countries and areas^c						
High	193 (36.0)	1029 (48.0)	1 (Reference)	...	1 (Reference)	...
Upper middle	108 (20.2)	566 (26.4)	1.02 (.79–1.32)	.90	1.33 (.94–1.89)	.11
Lower middle	227 (42.4)	542 (25.3)	2.23 (1.79–2.79)	<.001	2.46 (1.69–3.58)	<.001
Low	8 (1.5)	7 (0.3)	6.09 (2.17–17.12)	<.001	7.25 (2.22–23.66)	.001
Any symptoms						
No	528 (98.5)	2136 (99.6)	1 (Reference)	...	1 (Reference)	...
Yes	8 (1.5)	8 (0.4)	4.05 (1.51–10.85)	.003	4.08 (1.43–11.65)	.009
Specimen type						
Saliva	451 (84.1)	1989 (92.8)	1 (Reference)	...	1 (Reference)	...
Nasopharyngeal	85 (15.9)	155 (7.2)	2.42 (1.82–3.22)	<.001	2.75 (1.85–4.09)	<.001
Use of travel corridor framework						
No	504 (94.0)	1912 (89.2)	1 (Reference)	...	1 (Reference)	...
Yes	32 (6.0)	232 (10.8)	0.52 (.36–.77)	<.001	0.48 (.30–.77)	.002
Seafarer						
No	432 (80.6)	1893 (88.3)	1 (Reference)	...	1 (Reference)	...
Yes	104 (19.4)	251 (11.7)	1.82 (1.41–2.34)	<.001	0.81 (.56–1.18)	.27

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; OR, odds ratio; WHO, World Health Organization.

^aAdjusted for all other explanatory variables presented in this table.

^bTravelers with both Japanese and non-Japanese nationalities were classified as non-Japanese.

^cCountries and areas where travelers stayed within 14 days before arrival.

additional easing measure for students, dependents, and others was introduced on 1 October, this number further increased substantially. By contrast, the COVID-19 test positivity slightly decreased. Furthermore, the positivity was lower in travelers using travel corridor frameworks, including pretravel tests, than in other travelers. Although there is little information on

how to lift travel restrictions safely, a simulation study showed that PCR tests within 3 days of departure and rapid antigen detection tests on the day of travel reduced the number of infectious days by 36% and 32%, respectively [19]. Because travel corridor users in our study were screened even on arrival, the framework could further reduce transmission risk.

Children and adolescents (aged 3–19 years) and female travelers were less likely to test positive for COVID-19 than adults and male travelers, respectively. These results are consistent with previous studies reporting virus prevalence or seroprevalence [20–23]. A national prevalence study from Iceland reported that children aged ≤ 10 years and females had lower COVID-19 incidence rates than adolescents or adults and males, respectively [21]. Another population-based study in Geneva, Switzerland, reported that children aged 5–9 years and females had a significantly lower risk of being seropositive than adults aged 20–49 years and males, respectively [22]. Whether the lower prevalence in these 2 groups resulted from less exposure to the virus or biologic resistance remains unclear [24], although the lower prevalence in children might be partially related to lower nasal gene expression of angiotensin-converting enzyme 2, the receptor that SARS-CoV-2 uses for host entry [25, 26].

Our study showed that COVID-19 test positivity was higher among individuals aged 0–2 years than among those aged 3–19 years, even after adjustment for specimen type, because 92.0% of samples in children (3437 of 3737) were obtained using nasopharyngeal swabs owing to difficulties collecting saliva. Although the explanation remains to be elucidated, infants and younger children tend to touch various things around them and have difficulties adhering to protective measures, including wearing masks.

High COVID-19 test positivity was also associated with severe epidemics and lower income levels in the countries and areas where the travelers stayed. The high positivity in travelers from low- and lower-middle-income countries could result from weak health systems, including the lack of an adequate surveillance system and laboratory testing capacity, or poor community hygiene and sanitation. A postmortem surveillance study from Zambia reported that deaths with COVID-19 were common particularly in communities where testing capacity was lacking [27]. Moreover, a study from Tanzania conducted before the COVID-19 pandemic reported poor compliance with infection prevention measures even in health facilities and particularly low compliance with hand hygiene, at 6.9% [28]. These issues that are common in lower-income countries also raise concern on underestimated COVID-19 impact and risk of decision making for easing travel restrictions based on the reported number of cases and deaths in lower-income countries.

Nasopharyngeal swab sampling was associated with higher COVID-19 test positivity, compared with saliva collection. This result is supported by a systematic review and meta-analysis, reporting by subgroup analyses that COVID-19 tests with saliva specimen had lower sensitivity than those with nasopharyngeal swab sampling among undiagnosed persons presenting for COVID-19 testing or those whose saliva was collected using a general spitting technique [29].

Our study has some limitations. First, there was a slight difference in screening test measures among airport and port

quarantine stations, which could introduce bias. However, >99% of all travelers were tested with the same strategy: confirmation with NAT if the result of a screening antigen detection test was inconclusive. Matching based on arrival airports or ports and arrival dates was also used to control for different screening strategies. Moreover, the sensitivity analysis suggested that the different screening measures had little effect on the results. Second, we could not obtain detailed information on travelers' symptoms to assess which symptoms are most helpful in COVID-19 screening. However, our findings showed that travelers with any symptoms on arrival were more likely to be COVID-19 positive.

Another possible limitation is using a quantitative antigen detection test rather than NAT, because the sensitivity and specificity of the antigen detection test used were 70.5%–100% and 99.3%–100%, respectively, compared with reverse-transcription PCR [14]. Although it can cause a relatively higher false-positive rate in low-prevalence settings, even NAT with higher sensitivity and specificity cannot achieve an acceptable positive predictive value in the setting [30]. Because the negative predictive value is high even in low-prevalence settings, an antigen detection test that is convenient for scaling up testing can be used with confidence at international borders for screening to rule out infection. Finally, we should take into account differences in the population targeted by border control measures. However, it is considered to improve the generalizability that this study included travelers from >170 countries and areas, accounting for 55.9% of all arrivals, and was conducted with arrivals nationwide.

In conclusion, the current study revealed high- and low-risk populations at airport and port quarantine stations and justified the travel restrictions based on the epidemic situation in countries of stay, although it is possible that the epidemic situation was underestimated in lower-income countries. Our results also highlight the reduced COVID-19 importation risk enabled by strict travel corridor frameworks, including pretravel and posttravel screening tests for safe reopening of international borders. These findings will guide governments to make evidence-based decisions when imposing or easing travel restrictions in the era of new SARS-CoV-2 variants.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. M. T. conceived the study; M. T., M. H., and H. O. designed the study; M. T. collected data; M. T. and H. O. performed analyses; and M. T. wrote the first draft of the manuscript. All authors reviewed the manuscript and agreed with its results and conclusions.

Acknowledgments. The authors thank the Ministry of Health, Labour and Welfare, Japan, for support and sharing of data collected at quarantine stations for use in their analyses.

Financial support. This work was supported by the Health, Labour and Welfare Policy Research Grants, Research on Emerging and Re-emerging Infectious Diseases and Immunization (grant 20HA2002).

Potential conflicts of interest. H. O. reports personal fees from EPS International as an external statistical consultant for clinical trial, outside the submitted work. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Han E, Tan MMJ, Turk E, et al. Lessons learnt from easing COVID-19 restrictions: an analysis of countries and regions in Asia Pacific and Europe. *Lancet* **2020**; 396:1525–34.
2. Air travel in the time of COVID-19. *Lancet Infect Dis* **2020**; 20:993.
3. Murphy N, Boland M, Bambury N, et al. A large national outbreak of COVID-19 linked to air travel, Ireland, summer 2020. *Euro Surveill* **2020**; 25:2001624.
4. Choi EM, Chu DKW, Cheng PKC, et al. In-flight transmission of SARS-CoV-2. *Emerg Infect Dis* **2020**; 26:2713–6.
5. Freedman DO, Wilder-Smith A. In-flight transmission of SARS-CoV-2: a review of the attack rates and available data on the efficacy of face masks. *J Travel Med* **2020**; 27:taaa178.
6. Khanh NC, Thai PQ, Quach HL, et al. Transmission of SARS-CoV 2 during long-haul flight. *Emerg Infect Dis* **2020**; 26:2617–24.
7. Dickens BL, Koo JR, Lim JT, et al. Strategies at points of entry to reduce importation risk of COVID-19 cases and reopen travel. *J Travel Med* **2020**; 27:taaa141.
8. Chinazzi M, Davis JT, Ajelli M, et al. The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. *Science* **2020**; 368:395–400.
9. Russell TW, Wu JT, Clifford S, Edmunds WJ, Kucharski AJ, Jit M; Centre for the Mathematical Modelling of Infectious Diseases COVID-19 working group. Effect of internationally imported cases on internal spread of COVID-19: a mathematical modelling study. *Lancet Public Health* **2021**; 6:e12–20.
10. Costantino V, Heslop DJ, MacIntyre CR. The effectiveness of full and partial travel bans against COVID-19 spread in Australia for travellers from China during and after the epidemic peak in China. *J Travel Med* **2020**; 27:taaa081.
11. Ministry of Justice, Japan. Regarding denial of landing to prevent the spread of COVID-19 (novel coronavirus), 28 June 2021. Available at: <http://www.moj.go.jp/isa/content/001347332.pdf>. Accessed 21 July 2021.
12. Ministry of Foreign Affairs of Japan. Phased measures for resuming cross-border travel, June 28 2021. Available at: https://www.mofa.go.jp/ca/cp/page22e_000925.html. Accessed 21 July 2021.
13. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* **2007**; 370:1453–7.
14. Pharmaceuticals and Medical Devices Agency. Lumipulse SARS-CoV-2 Ag [in Japanese]. Available at: https://www.info.pmda.go.jp/downloads/ivd/PDF/670773_30200EZK00035000_A_01_09.pdf. Accessed 21 July 2021.
15. Aoki K, Nagasawa T, Ishii Y, et al. Clinical validation of quantitative SARS-CoV-2 antigen assays to estimate SARS-CoV-2 viral loads in nasopharyngeal swabs. *J Infect Chemother* **2021**; 27:613–6.
16. World Bank Group. World Bank Country and Lending Groups. Available at: <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups>. Accessed 21 July 2021.
17. World Health Organization. WHO coronavirus disease (COVID-19) dashboard. Available at: https://covid19.who.int/?gclid=EA1aIQobChMirJLwxP_y7QIVymSLCh3dXgN4EAAYASAAEgLSzfd_BwE. Accessed 21 July 2021.
18. United Nations. Population division, world population prospects 2019. Available at: <https://population.un.org/wpp/>. Accessed 6 June 2021.
19. Kiang MV, Chin ET, Huynh BQ, et al. Routine asymptomatic testing strategies for airline travel during the COVID-19 pandemic: a simulation study. *Lancet Infect Dis* **2021**; 21:929–38.
20. Viner RM, Mytton OT, Bonell C, et al. Susceptibility to SARS-CoV-2 infection among children and adolescents compared with adults: a systematic review and meta-analysis. *JAMA Pediatr* **2021**; 175:143–56.
21. Gudbjartsson DF, Helgason A, Jonsson H, et al. Spread of SARS-CoV-2 in the Icelandic population. *N Engl J Med* **2020**; 382:2302–15.
22. Stringhini S, Wisniak A, Piumatti G, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study. *Lancet* **2020**; 396:313–9.
23. Tsuboi M, Hachiya M, Noda S, Iso H, Umeda T. Epidemiology and quarantine measures during COVID-19 outbreak on the cruise ship Diamond Princess docked at Yokohama, Japan in 2020: a descriptive analysis. *Glob Health Med* **2020**; 2:102–6.
24. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. *Pediatrics* **2020**; 145:e20200702.
25. Bunyavanich S, Do A, Vicencio A. Nasal gene expression of angiotensin-converting enzyme 2 in children and adults. *JAMA* **2020**; 323:2427–9.
26. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, et al; ENE-COVID Study Group. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet* **2020**; 396:535–44.
27. Mwananyanda L, Gill CJ, MacLeod W, et al. Covid-19 deaths in Africa: prospective systematic postmortem surveillance study. *BMJ* **2021**; 372:n334.
28. Powell-Jackson T, King JJC, Makungu C, et al. Infection prevention and control compliance in Tanzanian outpatient facilities: a cross-sectional study with implications for the control of COVID-19. *Lancet Glob Health* **2020**; 8:e780–9.
29. Bastos ML, Perlman-Arrow S, Menzies D, Campbell JR. The sensitivity and costs of testing for SARS-CoV-2 infection with saliva versus nasopharyngeal swabs: a systematic review and meta-analysis. *Ann Intern Med* **2021**; 174:501–10.
30. Peeling RW, Olliaro PL, Boeras DI, Fengwen N. Scaling up COVID-19 rapid antigen tests: promises and challenges. *Lancet Infect Dis* **2021**; doi:10.1016/S1473-3099(21)00048-7.